

## **REMARKS**

### Cancellation of Claims

Claims 5 and 7 are canceled without prejudice, waiver, or disclaimer. Applicants take this action merely to reduce the number of disputed issues and to facilitate early allowance and issuance of other claims in the present application. Applicants reserve the right to pursue the subject matter of these canceled claims in a continuing application, if Applicants so choose, and do not intend to dedicate any of the canceled subject matter to the public.

### Claims Rejections under 35 U.S.C. § 102

Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,620,898 to Yaremko. Applicants respectfully traverse.

Amended claim 11 recites the following: “a filter material chosen from at least one of the following: polyester mesh, nylon mesh, polycarbonate track-etched membrane, cellulose acetate membrane, and polyvinylidene difluoride filter membrane.” As noted by the Office, *Yaremko* teaches that “[t]he filter is made of either beads or a porous gel material.” *Office Action* at 2.

For at least this reason, all of the features of independent claim 11 are not taught or suggested by *Yaremko*. Applicants therefore respectfully request that the rejection be withdrawn.

### Claim Rejections under 35 U.S.C. § 103

Claims 1, 2-6, 8, 11, and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Yaremko* in view of U.S. Patent No. 5,308,990 to Takahashi. Claims 9 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Yaremko* and *Takahashi* and further in view of U.S. Patent No. 5,603,899 to Franciskovich. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Yaremko* and *Takahashi* and further in view of U.S. Patent No. 6,008,040 to Datar. Applicants respectfully traverse the rejections.

Claims 1, 11, and 25 are independent claims. As noted above, each of these independent claims has been rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over the combination of *Yaremko* in view of additional (secondary or tertiary) cited art. There is at least one fundamental distinction between the claimed embodiments of the present independent claims and *Yaremko*, which makes the rejections of the independent claims inapplicable. Specifically, the independent claims all recite “a filter material [or, “filter means” in claim 25] chosen from at least one of the following: polyester mesh, nylon mesh, polycarbonate track-etched membrane, cellulose acetate membrane, and polyvinylidene difluoride filter membrane.” Independent claims 1, 15, 16, and 22 have been amended herein to add this distinguishing feature, in an effort to advance the prosecution of this matter and further distinguish over the cited *Yaremko* patent.

In contrast to the independent claims, *Yaremko* does not disclose nor suggest such a filter. In fact, at column 6, lines 21-26, *Yaremko* teaches a different type of filter material. There, *Yaremko* states:

A multitude of very small, transparent glass beads, having diameters on the order of magnitude of 10 to 100 micrometers, are deposited in and form a filter in the lower portion of each microcolumn. Alternately, the lower portion of each microcolumn may be provided with a suitable gel that functions in the same general way as the microbeads.

*Yaremko* teaches beads or porous gel, because this type of filter is required to perform depth filtration, and thus separate cells through a thick filter. *Yaremko* uses a long-column containing gel or beads as a filter substance, with separation occurring within the column. The method of Yaremko would be unworkable using the filter materials recited in the present claims. For at least this reason, independent claims 1, 11, and 25 patently define over the cited art.

In fact, the Office Action admits that *Yaremko* admits that “[n]either Yaremko et al. nor Takahashi et al. teach the particular filter materials recited in claim 7 [now incorporated into claims 1, 11, and 25].” *Office Action* at 5. Instead, the Office Action relies on the teachings Datar (U.S. Patent 6,008,040) as supplying this teaching. Applicants respectfully disagree in part. Although *Datar* may disclose the use of

polyester, nylon, cellulose acetate, and PVDF, it does not teach or suggest the use of polycarbonate track-etched membrane.

In addition, *Datar* does not appear to be analogous to the present claims. *Datar* teaches how to separate different cell populations from one another using “cascade flow” of fluid. This has nothing to do with the instant application. The present claims do not recite separating different cells into distinct populations. Furthermore, *Datar* teaches depth filtration, where a thick filter medium (in their case made of multiple filter layers) is used for separation. In this way, separation occurs within the filter in *Datar*. In our the present independent claims, a membrane filter is recited with a pore size that retains cellular components or agglutinated components on top of the filter. Thus, not all of the teachings of the independent claims are taught or suggested by *Yaremko* and *Takahashi* in combination with *Datar*. Even combining the cited references would not lead one skilled in the art to abandon the depth filtration of *Yaremko* and *Datar* for the surface filtration recited in the independent claims. In light of this explicitly-claimed feature, the applied combination of *Datar* with *Yaremko* is inappropriate.

In addition, each of the independent claims have been amended to recite the feature of “the filter material including a plurality of pores with a pore size from about 3 microns to about 5 microns” in claim 1; “the filter material including a plurality of pores with a pore size from about 0.1 microns to about 3 microns” in claim 11; and “the filter means including a plurality of pores with a pore size from about 0.1 microns to about 3 microns” in claim 25. No where do any of the cited references teach or suggest the features of these pore sizes.

It is well settled law that in order to properly support an obviousness rejection under 35 U.S.C. § 103, there must have been some teaching *in the prior art* to suggest to one skilled in the art that the claimed invention would have been obvious. *W. L. Gore & Associates, Inc. v. Garlock Thomas, Inc.*, 721 F.2d 1540, 1551 (Fed. Cir. 1983). More significantly,

"The consistent criteria for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this [invention] should be carried out and would have a reasonable likelihood of success, viewed in light of the prior art. ..." Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's

disclosure... In determining whether such a suggestion can fairly be gleaned from the prior art, the full field of the invention must be considered; for the person of ordinary skill in the art is charged with knowledge of the entire body of technological literature, including that which might lead away from the claimed invention."

*In re Dow Chemical Company*, 837 F.2d 469, 473 (Fed. Cir. 1988) (Emphasis added).

In this regard, Applicants note that there must not only be a suggestion to combine the functional or operational aspects of the combined references, but that the Federal Circuit also requires the prior art to suggest *both* the combination of elements *and* the structure resulting from the combination. *Stiftung v. Renishaw PLC*, 945 Fed.2d 1173 (Fed. Cir. 1991). Therefore, in order to sustain an obviousness rejection based upon a combination of any two or more prior art references, the prior art must properly suggest the desirability of combining the particular elements to create the immunological assay system with *all* of the features as claimed by the Applicants.

When an obviousness determination is based on multiple prior art references, there must be a showing of some "teaching, suggestion, or reason" to combine the references. *Gambro Lundia AB v. Baxter Healthcare Corp.*, 110 F.3d 1573, 1579, 42 USPQ2d 1378, 1383 (Fed. Cir. 1997) (also noting that the "absence of such a suggestion to combine is dispositive in an obviousness determination").

Evidence of a suggestion, teaching, or motivation to combine prior art references may flow, *inter alia*, from the references themselves, the knowledge of one of ordinary skill in the art, or from the nature of the problem to be solved. *See In re Dembiczak*, 175 F.3d 994, 1000, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999). Although a reference need not expressly teach that the disclosure contained therein should be combined with another, the showing of combinability, in whatever form, must nevertheless be "clear and particular." *Dembiczak*, 175 F.3d at 999, 50 USPQ2d at 1617.

If there is motivation or suggestion to combine selective teachings from multiple prior art references, one of ordinary skill in the art would not have viewed the present invention as obvious. *See In re Dance*, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998); *Gambro Lundia AB*, 110 F.3d at 1579, 42 USPQ2d at 1383 ("The

absence of such a suggestion to combine is dispositive in an obviousness determination.”).

Significantly, where there is not apparent disadvantage present in a particular prior art reference, then generally there can be no motivation to combine the teaching of another reference with the particular prior art reference. *Winner Int'l. Royalty Corp. v. Wang*, No 98-1553 (Fed. Cir. January 27, 2000).

Simply stated, the application of the combination of *Yaremko* with *Takahashi* and *Datar* against the independent claims of the present application is inappropriate, and for at least the forgoing reasons, Applicants respectfully submit that the rejections should be withdrawn for at least these reasons. Having set forth the forgoing, the undersigned will, below, address each independent claim.

(a) Independent Claim 1

The Office Action has rejected claim 1 as allegedly unpatentable over the combination of *Yaremko* in view of *Takahashi*. For at least the reasons that follow, Applicants respectfully disagree and request that the rejection be withdrawn.

Independent claim 1, as amended, recites:

1. An immunological assay system, comprising:
  - a filter vessel capable of containing ***an assay sample of red blood cells, white blood cells, or platelets, wherein the filter vessel comprises a filter material chosen from at least one of the following: polyester mesh, nylon mesh, polycarbonate track-etched membrane, cellulose acetate membrane, and polyvinylidene difluoride filter membrane, the filter material including a plurality of pores with a pore size from about 3 microns to about 5 microns;***
  - an incubator in which the filter vessel may be placed, wherein the incubator houses the filter vessel while the assay sample and one or more ***reagent antibodies*** react;
  - a sample separation system in close proximity to the incubator, wherein the sample separation system is designed to separate the mixture of the assay sample and the reagent antibodies into various components;
  - an image acquisition system in close proximity to the sample separation system, wherein the image acquisition system consists of a flow cytometer, ***the flow cytometer being designed to detect the presence of interactions between reagent antibodies and the assay sample cells,*** wherein said interactions are evidenced by at least one of agglutinations and antigen-antibody interactions; and

a robotic pipettor including a robotic arm within reaching distance of the filter vessel, the incubator, the sample separation system and the image acquisition system, wherein the robotic pipettor is designed to transfer the assay sample or the reagent antibodies between the filter vessel, incubator, the sample separation system and the image acquisition system.

(*Emphasis added*). Applicants respectfully submit that independent claim 1 defines over the combination of *Yaremko* and *Takahashi* for at least the reason that the combination fails to teach the features emphasized above. Specifically, as noted above, the cited references (including *Datar*) fail to teach or suggest the feature of “wherein the filter vessel comprises a filter material chosen from at least one of the following: polyester mesh, nylon mesh, polycarbonate track-etched membrane, cellulose acetate membrane, and polyvinylidene difluoride filter membrane, the filter material including a plurality of pores with a pore size from about 3 microns to about 5 microns.”

In addition, *Yaremko* fails to teach or suggest the recited feature of claim 1 of “flow cytometer being designed to detect the presence of interactions between reagent antibodies and the assay sample cells” and the assay sample including “red blood cells, white blood cells, or platelets.” Indeed, the Office admits this by stating, “*Yaremko et al.* differs from the instant invention in that it teaches a camera to image the analysis results, whereas Applicants claim the use of a flow cytometer.” *Office Action* at 4. *Takahashi* fails to cure this deficiency. The portion of *Takahashi* relied on by the Office, col. 1, lines 37-53 discloses the following:

On the other hand, as an immunological measurement method using particles, there is known a method, by which ***antigen concentration is measured by making latex spheres, with the surface of which an antibody is bound***, react with an antigen and ***measuring the agglutinated state of the latex spheres*** produced by the antigen-antibody reaction by the absorbance or the intensity of scattered light. Further, in order to analyze this agglutinated state with a high precision, there is known also a method, by which each agglutinated lump is led to a flow cytometer to be analyzed there. By this method it is possible to calculate the magnitude of each agglutinated lump, based on the intensity of scattered light to measure the antigen concentration with a high precision...

(*Emphasis added*). Thus, the disclosure of *Takahashi* is limited to measuring the agglutinated state of latex spheres to which antibodies are bound. Essentially, *Takahashi* simply describes using a flow cytometer to count the latex beads. Nothing in *Takahashi* teaches or suggests detecting interactions of a patient assay sample and reagent antibodies that are not bound to latex spheres.

Not only is *Takahashi* limited to measuring agglutinated state of latex spheres (not antigen-red blood cell interactions, *e.g.*, as in the independent claims), but *Takahashi* does not require filter materials since their assays do not require separation of cells from fluid. The filter of the independent claims is of a pore size the filters cellular components from fluid.

In addition, Applicants respectfully submit that the combination of *Yaremko* with *Takahashi* is improper. *Yaremko* is directed to an automated blood analysis system, whereas *Takahashi* is directed to a method and instrument “for measuring microparticles *capable of detecting microparticles having a very low fluorescence intensity existing in liquid...*” *Id.* at col. 1, lines 8-11 (*emphasis added*). The field of immunological testing is very broad. One searching for a solution to any problems of *Yaremko* would not look for answer in *Takahashi* because *Takahashi* is directing to detecting microparticles having an inherent fluorescence. In addition, it does not teach filtration or the use of filters to prepare cells for this process. No where does *Yaremko* teach or suggest detecting microparticles having an inherent fluorescence. Thus, these two references are directed to very different aspects of the broad field of immunological testing.

For at least these reasons, as well as the reasons recited above, Applicants respectfully submit that the combination of *Yaremko* and *Takahashi* does not render claim 1 obvious, and request that the rejection of claim 1 be withdrawn.

(b) Independent Claim 11

The Office Action rejected claim 11 on the same identical bases as claim 1 (see Office Action, pages 3-4). The undersigned respectfully submits that such a rejection is inappropriate, as the two claims are not coextensive in scope. However, for purposes of

this response, and in an effort to advance the prosecution of this application, the undersigned submits that claim 11 patently defines over the cited art for at least some of the same reasons discussed above in connection with claim 1. In this regard, claim 11 includes the features of “a filter material chosen from at least one of the following: polyester mesh, nylon mesh, polycarbonate track-etched membrane, cellulose acetate membrane, and polyvinylidene difluoride filter membrane”, which is not taught or suggested by the cited references.

In addition, claim 11 recites the feature of “the filter material including a plurality of pores with a pore size from about 0.1 microns to about 3 microns.” This feature is also not taught or suggested by the cited references.

For at least these reasons, as well as the reasons recited above, Applicants respectfully submit that the combination of *Yaremko* and *Takahashi* does not render claim 11 obvious, and request that the rejection of claim 11 be withdrawn.

(c) Independent Claim 25

The Office Action rejected claim 25 on the same identical bases as claim 1 (see Office Action, pages 3-4). The undersigned respectfully submits that such a rejection is inappropriate, as the two claims are not coextensive in scope. Although there are distinctions between claims 25 and claim 1, the filter means of claim 25 is chosen from at least one of the following: polyester mesh, nylon mesh, polycarbonate track-etched membrane, cellulose acetate membrane, and polyvinylidene difluoride filter membrane, and the filter means includes a plurality of pores with a pore size from about 0.1 microns to about 3 microns, similar to a corresponding elements of claims 1 and 11. As noted above, these features are not taught or suggested by the recited references.

In addition, claim 25 recites a flow cytometer that is “configured to determine the presence of interactions between the antibodies and antigen carriers.” As noted above, *Yaremko* does not disclose a flow cytometer in its system. *Takahashi* discloses a flow cytometer that analyzes the agglutinated state of *latex spheres* to which antibodies are bound. Thus, using a flow cytometer to measure only naturally occurring cellular



components, as claimed in claim 25, is not taught or suggested by the combination of cited references.

For at least these reasons, as well as the reasons recited above, Applicants respectfully submit that the combination of *Yaremko* and *Takahashi* does not render claim 11 obvious, and request that the rejection of claim 11 be withdrawn.

Because independent claims 1 and 25 are allowable, then for at least this reason, their dependent claims 2-4, 6, 8-9, and 26-28 are also allowable. Applicants therefore respectfully request that the rejection of these claims be withdrawn as well.

### **CONCLUSION**

In light of the foregoing amendments and for at least the reasons set forth above, Applicants respectfully submit that all rejections have been traversed, rendered moot, and/or accommodated, and that the now pending claims 1-4, 6, 8-9, and 11-28 are in condition for allowance. Favorable reconsideration and allowance of the present application and all pending claims are hereby courteously requested. If, in the opinion of the Examiner, a telephone conference would expedite the examination of this matter, the Examiner is invited to call the undersigned attorney at (770) 933-9500.

Respectfully submitted,

  
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